Tranexamic Acid(cyclokapron) for Reducing Perioperative Blood Loss Associated With Total Knee Arthroplasty

Thesis

Submitted in partial fulfillment for the M.D. degree in anesthesia and ICU

BY

Khaled Mohamed Abdallah abdalsalam

M.Sc.-Arab Board

Supervisors

Prof. Dr/ Bahira M. Tawfeik
Prof. Of anesthesiology & ICU
Ain Shams University

Prof. Dr/ Madiha Metwaly
Prof. Of anesthesiology & ICU
Ain shams University

ASS. Prof. Dr/ Adel Ahmed Fathi
Ass.Prof. Of anesthesiology & ICU
Ain shams University

Dr/ Halah Gomah Salama
Lecturer Of anesthesiology & ICU
Ain shams University

Faculty of Medicine
Ain Shams university
2001


بسم الله الرحمن الرحيم
سبحانك
لا علم لنا إلا ما علمتنا إنك أنت العليم الحكيم
صدق الله العظيم
سورة البقرة آية ٣٢

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To My Family

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Introduction

INTRODUCTION

Total knee arthroplasty (TKA) has become a reliable surgical procedure to treat painful degenerative arthritis. Pain relief and functional improvement are excellent, and can allow the patient to maintain active life style **(Rathjen, 1998).** Heavy bleeding that occurs following TKA, is often difficult to control **(Martin et al., 1998).**

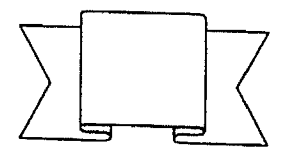
Many statistical studies have been done to evaluate blood loss and the use of homologous blood transfusion following TKA .In 1996, **Bierbaum and his colleagues** conducted a study to evaluate transfusion requirements, associated with total joint arthroplasty; a total of 9482 patients were evaluated prospectively from September, 1996 till June, 1997. Four thousand and four hundred and nine (46%) patients required blood transfusion. The frequency of allogenic blood transfusion was found to vary with respect to the type of surgical procedure, revision total hip arthroplasty and bilateral total knee arthroplasty were found to be associated with the highest prevalence of such transfusion **(Bierbaum et al., 1996).**

Various methods and great efforts have been tried to reduce bleeding, and avoid blood transfusion with all its complications.

Thorpe and his colleagues (1994) have studied the effect of aprotinin on blood loss and subsequent blood transfusion in patients undergoing knee replacement surgery. They concluded that, the role of aprotinin under tourniquet conditions is unclear.

Marmor used autogenous fibrinogen cryoprecipitate **in 1991**, to coat the operative site with a fibrin clot to determine the effect on postoperative blood loss A method of determining the inapparent blood loss was used, based on the red cell mass of the patient. The magnitude of tissue extravasation was surprising, and it was almost double the blood loss expected by traditional methods. The benefit of using fibrinogen concentrates is exclusively confined to the inapparent blood loss and not the postoperative blood loss **(Marmor et al., 1991).**

Akizuki tried a new method for hemostasis during cementless TKA. He injected tranexamic acid locally in the wound through the drain tube, which was clamped for about 30 minutes after deflation of the tourniquet. Blood loss and transfusion requirements were reduced markedly **(Akizuki et al., 1997).**



Review of Literature

HEMOSTASIS

Hemorrhage and thrombosis are two major problems which affect the outcome of surgery **(Gordon, 1995).** To meet the requirements of interdependent tissues with high metabolic activities, the circulation must be rapid and within a closed circulatory system High blood velocity is achieved as a result of high pressure, but since a high pressure system is specially vulnerable to leakage, it is essential that bleeding due to injured blood vessels is arrested rapidly **(Patricia,1996).** The process of hemostasis, which is the spontaneous arrest of blood loss from ruptured vessels, fulfills this requirement **(Richard et al., 1996).**

Hemostasis involves interactions among damaged blood vessel wall, platelets, and circulating blood coagulation factors. This interaction results in constriction of the blood vessel wall, and Formation of a hemostatic plug which prevents further blood loss **(Figure 1) (Bloom and Fawcett, 1994)**

Vascular constriction

Immediately after a blood vessel is cut or ruptured, the stimulus of the traumatized vessel causes the wall of the vessel to contract; this instantaneously reduces the flow of blood from the vessel rupture. The contraction results from nervous reflexes, local myogenic spasm, and local humoral factors from the traumatized tissues and blood platelets. The nervous reflexes presumably are initiated by pain or other impulses originating from the traumatized vessel or from nearby

tissues. However, much of the vasoconstriction probably results from local myogenic contraction of the blood vessels initiated by direct damage to the vascular wall. For the small vessels, the platelets are responsible for much of the vasoconstriction by releasing the vasoconstrictor substance ***thromboxane A2.*** The more vessel traumatized, the greater the degree of spasm, this means that a sharply cut blood vessel usually bleeds much more than does a vessel ruptured by crushing. This local vascular spasm can last for many minutes or even hours, during which time the ensuing processes of platelet plugging and blood coagulation can take place.

The value of vascular spasm as a mean of hemostasis is illustrated by the fact that, persons whose legs have been severed by crushing types of trauma, sometimes have such intense spasm in vessels as large as the anterior tibial artery. That, there is no lethal loss of blood **(Guyton, 2000).**

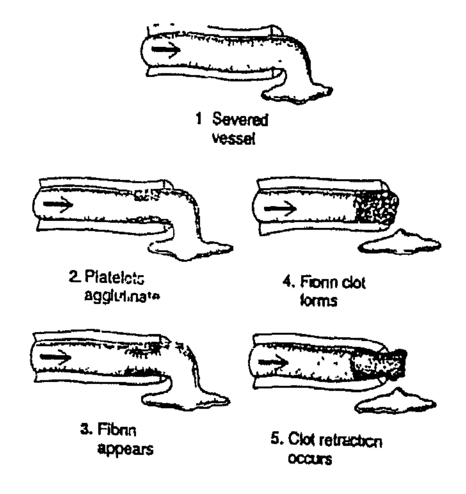


Figure 1: Summary of reactions involved in hemostasis **(Guyton & Hall, 2000).**

Formation of the platelet plug

Platelets are small blood cells comprising 0.5percentage of the blood volume, and are synthesized in the bone marrow from megakaryocytes. The normal platelet life span is 5-7 days, and the normal count is 150,000-400,000/microliter **(Thomas, 1996).** Platelet membrane plays a key role in hemostasis. Platelets carry receptors, which respond to factors exposed or released by tissue injury, which lead to platelet adhesion and aggregation. The phospholipids of platelets provide structure on which activated coagulation factors are brought together in the optimum steriospecific fashion, for rapid conversion of Prothrombin to thrombin. Specific glycoproteins (GP) on the platelet surface are receptors for aggregating agents, coagulation factors and inhibitors **(Peter, 1995).** Platelet adhesion, is followed by platelet aggregation, as more cells come together at the same site forming a platelet plug. Another agent, which promotes platelet aggregation is thrombin, generated as a result of activation of the coagulation system. These cells contain large numbers of membrane enclosed granules, and dense bodies, but are not nucleated **(Smith, 1996).**

The platelet plug contracts and the contents of the large numbers of the intracellular membrane enclosed dense bodies are released within the plug and into the surrounding blood, this is the platelet release reaction. Among the contents released from the activated platelets are ADP and thromboxane A2 (which promote platelet aggregation), serotinin (5-hydroxytryptamine)(a vasoconstrictor) and

calcium ions **(William, 1999).** The platelet release reaction also results in the exposure of platelet phospholipid, and factor V, which have important roles in localizing subsequent coagulation events. The end result of this process is the creation of a hemostatic plug, consisting of platelets and fibrin, within which other blood cells are trapped **(Frojmovic, 1992).**

In summary, injury to blood vessels normally causes localized spasm as a result of the release of humoral factors (from platelets) as well as local myogenic reflexes. Sympathetic-mediated vasoconstriction is also probably operative in medium-sized vessels. Exposure of circulating platelets to the damaged endothelial surface causes them to undergo a series of changes that results in the formation of platelet plug ***(figure 2)*** **(Rodney, 2000).**

BLOOD COAGULATION:

The third mechanism for hemostasis is formation of the blood clot. The clot begins to develop in 15 to 20 seconds if the trauma to the vascular wall has been sever and in 1 to 2 minutes if the trauma has been minor. Activator substances, both from the traumatized vascular wall, and from platelets and blood proteins adhering to the traumatized vascular wall initiate the clotting process **(Guyton, 2000).** Within 3 to 6 minutes after rupture of a vessel, if the vessel opening is not too large, the entire opening or broken end of the vessel is filled with clot. After 20 minutes to an hour, the clot retracts; this closes the vessel still further. Platelets play an important role in this clot retraction **(Coller, 1991).**

Over 50 important substances that affect blood coagulation have been found in the blood and tissues, some promoting coagulation, called procoagulants, and others inhibiting coagulation. called anticoagulants. Whether or not the blood will coagulate depends on the degree of balance between these two groups of substances. Normally the anticoagulants predominate, and the blood does not coagulate, but when a vessel is ruptured, procoagulants in the area of damage become activated and override the anticoagulants, and then a clot does develop **(Williams, 1990).**

Formation of a Prothrombin converting factor

Coagulation may begin when blood comes in contact with injured tissue (the extrinsic pathway) or it may be initiated in the absence of tissue damage (the intrinsic pathway. When blood comes in contact with injured tissue, clotting is initiated via the extrinsic pathway, owing to the release of the tissue lipoprotein, thromboplastin (factor XIII). Tissue thromboplastin interacts with a plasma protein, proconvertin (factor VII), and calcium ions to form an agent that activates the stuart factor (factor X). The activated Stuart factor, in the presence of calcium ions, forms complexes with accelerin (factor V) on phospholipid micelles provided by tissue thromboplastin to form the Prothrombin- converting factor.

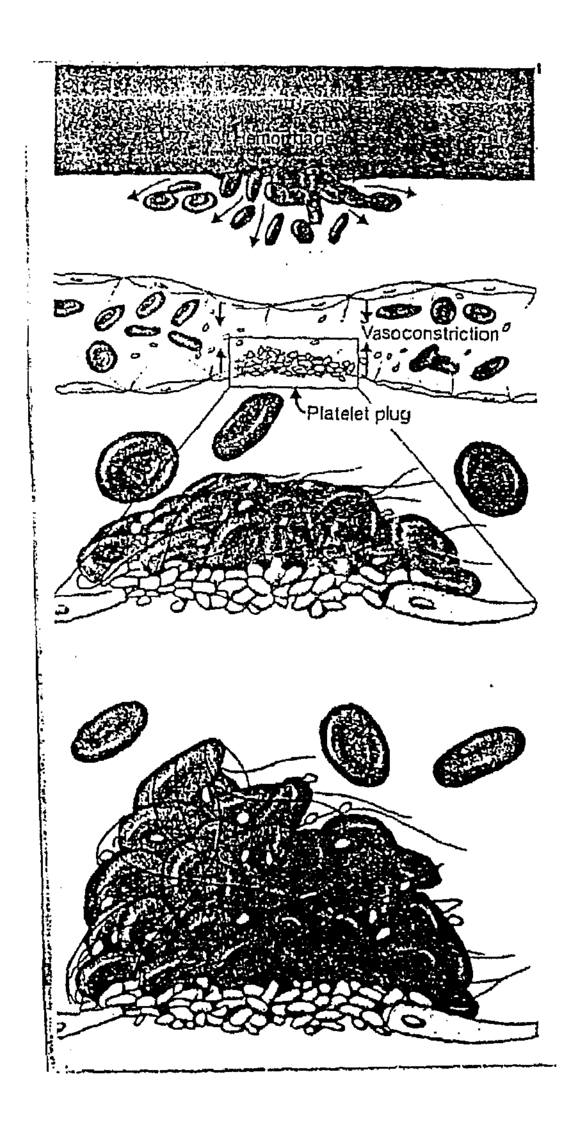


Figure 2: Formation of a blood clot. Fibrin forms long threads in which blood cells, platelets, and plasma become trapped **(Richard, 1996).**

Intrinsic coagulation may occur inside or outside of the body. In either case, the first step is the activation of the Hageman factor (factor XII). In the body, activation of the Hageman factor may occur from collagen, fibrin, or platelet membrane during platelet aggregation. In addition, it can apparently be activated under conditions of stress,

anxiety, fear, and other states. Outside the body (e.g. in a test tube), activation of the Hageman factor occurs when blood comes in contact with foreign substances whose common property appears to be a negative surface charge. The Hageman factor activates plasma thromboplastin antecedent (PTA), factor XI), which in the presence of calcium ions, activates a plasma protein, the Christmas factor (factor IX). Activated Christmas factor interacts with another protein, antihemophilic factor (factor VIII), on the surface of phospholipids and in the presence of calcium, to form a complex that activates the Stuart factor. The succeeding steps in the formation of Prothrombin converting factor are the same as for the extrinsic mechanism (Bloom,and Fawcett, 1994).

Conversion of Prothrombin to thrombin

Prothromin is a plasma globulin manufactured by the liver and normally present in plasma. It is the inactive precursor of an active enzyme called thrombin. Thrombin is not normally present in plasma unless blood is clotting ***(Figure 3).***

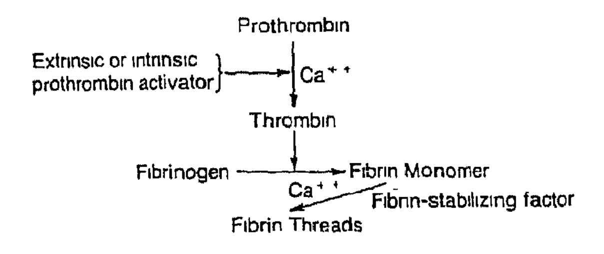


Figure 3: Conversion of Prothrombin to thrombin & Fibrinogen to fibrin (Richard, 1996).

Initially, the conversion of Prothrombin proceeds too slowly to produce significant amounts of thrombin needed for coagulation. Thrombin itself, however, increases its own rate of formation by converting a labile plasma protein, proaccelerin(factor V), into accelerin, which then accelerates the formation of thrombin. Thrombin also activates the antihemophilic factor and is needed to activate a fibrin-stabilizing factor **(Mann, 1989).**

Conversion of fibrinogen to fibrin

Fibrinogen is a soluble plasma protein produced by the liver and normally circulating in the plasma The proteolytic enzyme thrombin hydrolyses it, releasing two pairs of peptides, fibrinopeptides A and B, each with molecular weight of approximately 2000. The remaining molecule from which the fibrinopeptides have been cleaved is called fibrin. Its solubility is very low because fibrin molecules spontaneously aggregate through specific non-covalent interactions to form highly ordered fibrous polymer. Not only do fibrin molecules associate to form thick fibers, but more importantly also these fibers branch and create a three dimensional network with mesh size that is small enough to entrap erythrocytes. this network takes the form of a gel which is also capable of retaining for sometime the fluid portion of the blood **(Richard, 1996) (Figure 4).**

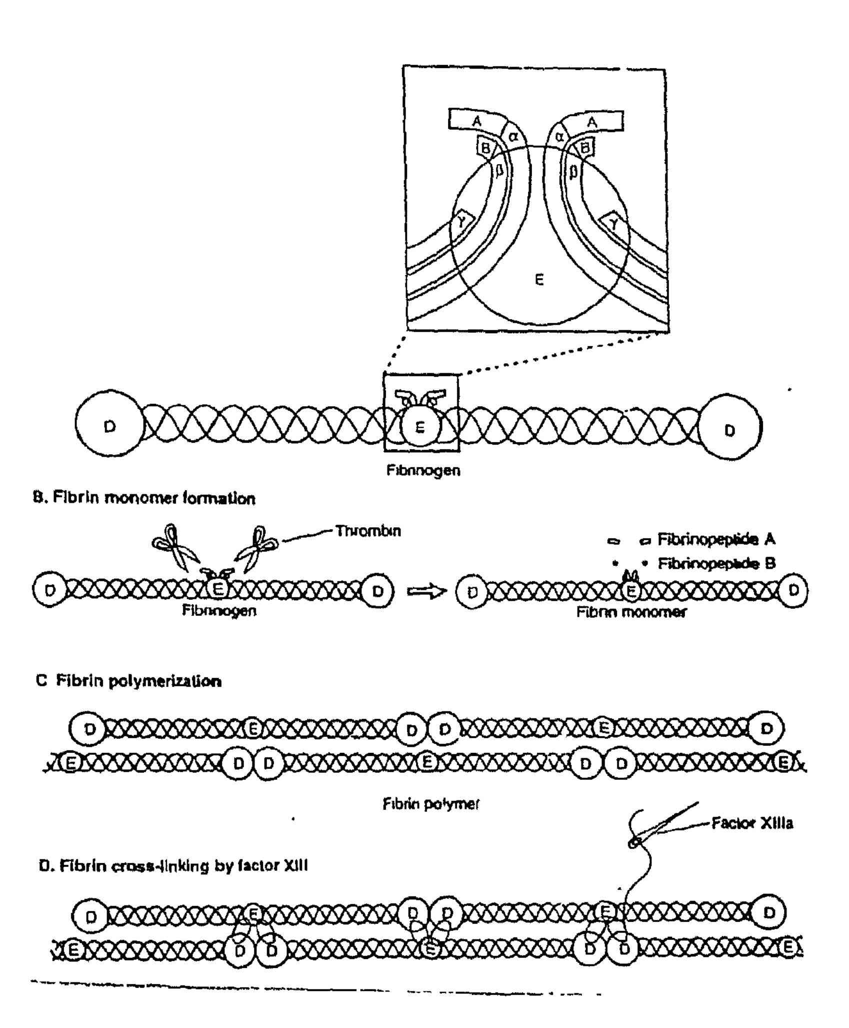


Figure 4: (A) Structure of fibrinogen. Six polypeptide chains, Two each of the A alpha, B beta, and gama chains are covalently linked to form a central E domain. The remainder of the chains coil outward to form the terminal D- domain. (B) Thrombin cleavage releases fibrinopeptide A&B thus transfoming fibrinogen to fibrin monomer. (C) Fibrin monomers polymerize and form fibrin gel. (D) Stabilization of fibrin (Richard, 1996).

FIBRINOLYSIS

Soon after coagulation is initiated, several regulatory mechanisms are activated, which ultimately inhibit coagulation. If left unchecked, the auto-amplification mechanisms of coagulation would result in generalized thrombosis *(Figure 5)* **(Patricia, 1996).**

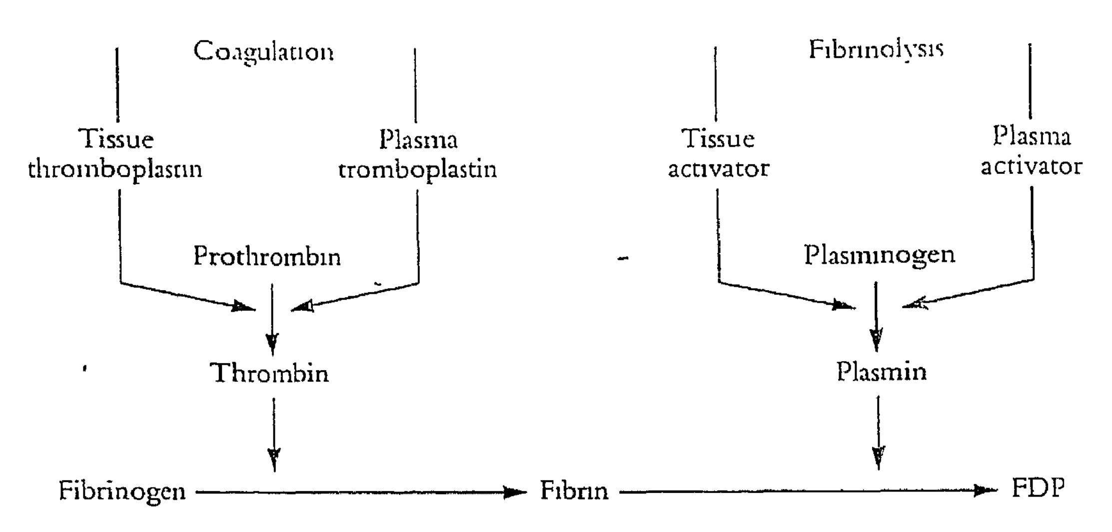


Figure 5: Hemostatic Equilibrium **(Rybo, 1991).**

Naturally occurring anticoagulants

Antithrombin III ; Antithrombin III currently is regarded as the most important physiologic inhibitor of coagulation. Antithrombin 3 is a plasma protein that acts as a serine protease inhibitor.

Activation: Although Antithrombin III inherently can inhibit the enzymatic activity of serine protease coagulation factors, the presence

of heparin increases this ability as much as 1000-fold(This is the predominant mechanism by which heparin acts as an anticoagulant.) Rather than true activation, heparin's effect on Antithrombin III is more accurately regarded as enhancement of preexisting activity. However, heparin does not naturally exist in plasma, which suggests that a heparin-like substance is responsible for enhancing the anticoagulant activity of Antithrombin III. This substance has been identified on the surface of endothelial cells and is called heparan sulfate.

Site of action; Antithrombin III can inhibit many serine protease enzymes (thrombin and factors Xa, IXa, and XIa) by forming one to one inactive complexes with them; however, thrombin's central role in coagulation makes this the most critical site of inactivation **(Thomas, 1996).**

Protein C; It is the inactive precursor form of the anticoagulant, protein Ca, which is a serine protease that acts on a specific clotting factors in the presence of the cofactor protein S. Both protein C and protein S are vitamin K-dependent.

Activation: Activation of protein C requires thrombin and thrombomodulin, a protein receptor found on the surface of endothelial cells. Interaction of thrombin and thrombomodulin causes a conformational change that greatly enhances thrombin effect on protein C, and inhibits its effects on fibrinogen and platelets.

Site of action:

- Coagulation; IN the presence of phospholipid and with protein S

as cofactor, protein Ca cleaves and inactivates factors Va and VIIIa, effectively disrupting the coagulation pathways.

- Fibrinolysis; With protein S as cofactor, protein Ca enhances fibrinolysis by preventing the degradation of plasminogen activator by its inhibitors.

Inactivation; Protein Ca activity is limited by another protein, protein C inhibitor **(Patricia et al., 1993).**

Other plasma protease inhibitors: These include:

Heparin cofactor 2, a heparin-activated protease inhibitor that acts on thrombin but not on factor 10a.

Alpha 2- Macroglobulin, which inhibits thrombin and various other proteases **(Guyton, 2000).**

Fibrinolytic system

In this system, the inactive precursor, plasminogen is converted to plasmin, a serine protease with specific fibrinolytic activity ***(figure 6).***

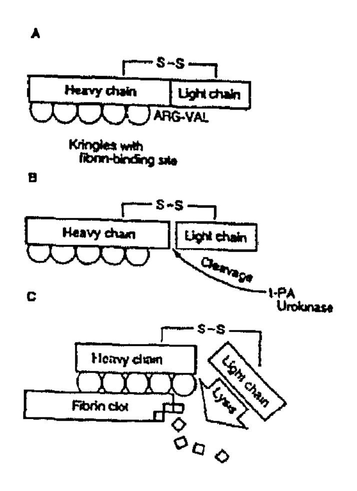


Figure6: (A)Plasminogen is a single-chain glycoprotein.(B)Inactive plasminogen is converted to plasmin.(C)Fibrinplytic activity is localized on light chain**(Patricia, 1993)**

FIBRIN DEGRADATION:

The formation and dissolution of fibrin leads to the production of various fibrin peptides, which have regulatory, diagnostic and therapeutic implications. Fibrinogen consists of two identical subunits, each consisting of three dissimilar peptides, alpha, beta, and gamma . Plasmin degrades fibrin into a number of fragments, which are, collectively, the fibrin degradation products (FDPs). Fibrin degradation products inhibit the conversion of fibrin monomers to fibrin polymers, fibrin to fibrinogen, and have anticoagulant properties themselves **(gordon, 1995).**

Laboratory studies

Ideally, the history and physical examination of the patient **(Table 1)** guide the choice of laboratory studies. However, for general screening purposes or when the history and examination provide no clues, a battery of appropriate tests often is the most expedient approach.

Platelet tests

Platelet count determination is the first step in evaluating disorder of primary hemostasis. Abnormal platelet count must be confirmed by peripheral blood smear.

Bleeding Time (BT)

Bleeding time is the time it takes for a clot to form after cuts have

been made on the forearm under controlled conditions. Normal bleeding time is 3-8 minutes. Prolongation of the bleeding time indicates abnormalities of platelet function or number. The bleeding time is difficult to perform because of problems in standardizing the conditions and should be carried out by the hemostasis staff **(Hunt, 1991).**

Tests of coagulation

Screening tests of coagulation must always be interpreted in light of the clinical situation. Abnormalities of hemostatic pathways may be measured using appropriate screening tests, that is, tests which measure the results of interference at any one or more of a number of steps along a defined pathway, rather than specific reaction or factor concentration.

Prothrombin Time (PT)

The Prothrombin time measures the integrity of the so-called extrinsic clotting pathway, including factor VII and the common pathway factors V, X, Prothrombin and fibrinogen. Thromboplastin is added in the form of brain extract to initiate the reaction. Variation in the thromboplastin has led to formulation of the international normalization ratio (INR) for the control of oral anticoagulant therapy. The normal PT is 10-14 seconds **(Thomas, 1996)**

Inquiry	Actions to be taken if response is positive
Past or recent history of bleeding or bruising	Blood count. Coagulation screen. Advice of hemostasis team
Family history of bleeding	Blood count. Coagulation screen. Advice of hemostasis team
Drug history	Warfarin(Discontinue 72 hours preoperatively. Use heparin if necessary. In emergency reverse with FFP+/-Vitamin K), Aspirin(Discontinue 72 hours preoperatively. Give platelets if bleeding excessive)
Past or family history of thrombosis	LMW heparin should be used in all high risk situations
Contraceptive pills	Stop 4 weeks prior to elective surgery, for emergency surgery use LMW heparin prophylaxis

Table 1: Inquiries relevant to hemostasis to be made preoperatively **(Gordon, 1995).**

Activated Partial Thromboplastin Time (APTT)

This measures the integrity of the intrinsic clotting pathway including factors VIII, IX, (XI-XII) as well as V, X, Prothrombin and fibrinogen. Normal APTT time is 30-40 seconds before a clot first forms **(Beverley & Heidi, 1999).**

Thrombin Time(TT)

Thrombin time is sensitive to deficiency or functional abnormality of fibrinogen and to inhibitors of thrombin activity including the presence of FDPs. The normal range is 15-16 seconds Heparins prolong the TT **(Gordon, 1995).**

Screening tests for coagulation pathways should be requested preoperatively if there is a worry concerning hemostasis abnormalities from the history or if the patient is known to have a disease, which may interfere with hemostasis. It is also essential to do screening tests if the patient is going to receive preoperative heparin, or the patient is to have emergency surgery and the history is not available .

Fibrin degradation products(FDPs)

Sometimes known as D-dimer test. Fibrin degradation products are the products of fibrin digestion by the fibrinolytic system. Their level is increased when a clot is formed, for example in pulmonary emboli and postoperatively, as well as in DIC (Beverley & Hunt., 1999).

Thromboelastography

Thromboelastography produces a quick global picture of hemostasis, including fibrinolysis. It measures the development of blood clot viscoelastic strength over time **(Saleem et al, 1988).**

THROMBOEMBOLISM

Formation of a clot inside a blood vessel is called thrombus to distinguish it from normal extravascular clotting of blood. An embolus is a fragment of the thrombus that breaks off and travels in the blood until it lodges at a site of vascular narrowing **(Timothy & Kevine,1995)**

Prophylaxis Against D.V.T.

The threat of venous thrombosis and acute pulmonary embolism (i.e. venous thromboembolism) is an everyday concern in the care of immobile patients. A variety of clinical conditions, can be accompanied by venous thrombosis in the lower extremities. Thrombosis involving the deep venous system in the thighs is often a silent process, and becomes evident only when it sends thrombotic projectiles to the lungs. In more than two thirds of cases of acute pulmonary embolism, the source of the problem (i.e. proximal leg vein thrombosis) goes unnoticed before the pulmonary embolism becomes developed **(Weinmenn &Salzman , 1994).** Because this thrombosis is such an insidious process, emphasis is placed with venous thromboembolism. Two words best characterize the mortality and morbidity due to venous thromboembolism; substantial and unacceptable **(Kenneth, 1990).**

Risk factors:

The clinical conditions that predispose to venous thromboembolism are summarized in **table 2**

♦ *Surgery:*

Several factors promote thrombosis in the early period following major surgery. These include venous stasis, vascular injury and a generalized hypercoagulable state caused by thromboplastins release during surgery and depressed levels of Antithrombin III that persist for five to seven days after surgery. Orthopedic procedures involving the hip and knee represent a particularly high risk for thromboembolism as does cancer related surgery in abdomen and pelvis **(Murphy,1995).** Parmet and his colleagues showed that, the incidence of large venous emboli in cases of total knee arthroplasty is high, and the use of tourniquet in this surgery, places the patients at a 5.33-fold greater risk of having a large emboli **(Parmet et al., 1998).** Patients who undergo prolonged abdomino-pelvic surgery or surgery to the lower limbs (total knee replacement), particularly if they require a period of reduced mobility postoperatively, are at high risk of venous thrombosis and embolism **(Collins et al., 1988).**

♦ *Medical illness:*

Relatively few acute medical illnesses carry a risk of venous thromboembolism. The most noted high-risk medical conditions are acute myocardial infarction, ischaemic stroke, lower extremity paralysis and cancer, particularly pelvic tumors. Trauma carries the same risk factors for thromboembolism as surgery (surgery is a form of controlled trauma). The high-risk conditions in trauma include multisystem involvement, Acute spinal cord injury, and fractures involving the pelvis and lower extremities **(Paul, 1999).**

Related to venous stasis	Thrombophilic states
Immobility	Hereditary
Dehydration	Antithrombin III deficiency
Cardiac failure	, Protein C, or S Deficiency
Stroke	Acquired
Pelvic obstruction	Lupus anticoagulant,
Nephrotic syndrome	Paroxysmal nocturnal hemoglobinuria,
Varicose veins	Pregnancy and puerperium,
Hypervicosity	oestrogens ,Surgery,
Sickle cell disease	Malignancy,
Age, Obesity, Sepsis	Major trauma

Table 2: Risk factors for thromboembolism **(Gordon, 1995).**

Methods of Prophylaxis:

A variety of preventive measures have proven effective in reducing the incidence of thromboembolism in bed-ridden patients. As a result, routine thromboprophylaxis is recommended for all patients in moderate and high-risk categories **(claggett et al, 1992).**

Graded Compression Stocking:

Graded compression stocking (also known as thrombo- embolism different or TED stockings) promote venous flow in the legs by providing 18 mmHg external compression at the ankles and 8mmHg external compression at the thigh **(Goldhaber et al., 1992).** These stockings have proven effective in reducing the incidence of Thromboembolism associated with major abdominal surgery and neurosurgery **(Wells et al.,1994).**

Intermittent Pneumatic Compression Boots:

Intermittent pneumatic compression boots are inflatable devices that provide 30-mmHg external compression at the ankles and 20-mmHg external compression at the thigh. These devices are considered more effective than graded compression stockings, and can more than double the venous flow rate in the legs. Because there is no risk of bleeding with pneumatic boots, they are favored in neuro-surgical patients and in patients undergoing prostatectomy. Pneumatic boots are also very effective in patients undergoing reconstructive surgery of the knee, and can be used as the sole prophylactic measure in these patients if there is no interference from immobilization casts **(Clagget et al.,1992).**

Anticoagulants:

Anticoagulants may be divided into several groups on the basis of their chemical structure, mechanism of action, and onset and duration of effect. Heparin and heparnoids are anticoagulants of direct and swift action. It binds to platelets and inhibits factors II, IX, X, XI & XII. Heparin is a physiological anticoagulant, which is produced in basophilic granules of mast cells in different organs and tissues and also outside mast cells. Heparin is not a single drug substance but a range of mucopolysaccharides, extracted from animal materials **(Hirsh et al., 1992).**

Low Dose Heparin:

The major anticoagulant action of heparin is to activate Antithrombin III, which then inhibits the conversion of Prothrombin

to thrombin. In the absence of active thrombosis, this action occurs at low doses of heparin, below the doses that interfere with other components of the coagulation process As a result, low doses of heparin can inhibit thrombus formation without creating the risk of hemorrhage associated with full anticoagulation **(Hirsh et al.,1992).**The usual low-dose heparin regimen is 5000 i.u subcutaneously every 12 hours, starting from the night of the day of surgery, and therapy continues through the first post-operative week or until the patient is ambulatory. Low-dose heparin is recommended as effective prophylaxis in major abdominal surgery and in acute medical illnesses with a risk of thromboembolism. It does not provide optimal prophylaxis in high-risk traumatic and orthopedic conditions **(Hirsh & Levine 1992).**

Low-Molecular Weight Heparin:

Low-molecular weight (LMW) heparin has more anticoagulant activity and produces an anticoagulant effect at lower dosages than the conventional unfractionated heparin**(Howard & Aaron, 1998).** The potential advantages of low-molecular weight heparin over unfractionated heparin include less frequent dosing, lower risk of bleeding, and a lower incidence of heparin-induced thrombocytopenia. At present, many of those advantages are more theoretical than actual. The disadvantage of low- molecular weight heparin is its cost, that is about 10 times more than that of unfractionated heparin **(Warkentin et al., 1995).** For enoxaparin (clexane, Rhone-Poelence Rorer pharmaceutical), the dosage for thromboprophylaxis is 30 mg

subcutaneous every 12 hours. Laboratory tests of coagulation status are not necessarily to be monitored Low molecular weight heparin is more effective than low-dose heparin in hip fractures, reconstructive surgery of the hip and knee, and the acute spinal cord injury with paralysis. It is not recommended in patients with active bleeding, or in documented cases of heparin-induced thrombocytopenia **(Warkentin et al., 1995).**

Low-Dose Warfarin:

Low-level anticoagulation with coumadine is an effective alternative to low-molecular weight heparin in patients with a high risk of thrombo-embolism. However, prophylaxis with coumadin is more cumbersome than with low-molecular weight heparin because it requires dosage titration and monitoring of laboratory tests of coagulation status **(Lieberman, 1999).**

Blood Loss In Total Knee Arthroplasty

Orthopedic operations rarely compromise the function of major organ systems in the way that invasive neuro-surgical, abdominal, cardiac or thoracic procedures may. Therefore, relatively few patients die as an immediate result of orthopedic surgery, provided that they receive minimally competent care from their surgeons and anesthetists. Nevertheless, these patients gain much from skilful management of their anesthetics, enhanced patient comfort, ***fewer blood transfusion, lessened risk of thromboemboli***, fewer and less

severe episodes of hypotension and hypertension **(Murphy, 1995).**

During orthopedic procedures, most blood is lost from raw bone and muscle surfaces rather than from identifiable blood vessels. This limits the surgeon's ability to control bleeding directly, allows much of the shed blood to escape collection by the suction catheters or gauze sponges, and ensures that bleeding continues after the wound is closed **(postoperative blood loss).** Surgeons and anesthetist almost always underestimate blood loss. Radioisotope study of blood loss in major orthopedic procedures showed that estimates of loss were, on average, 50% of the true measured losses.

When blood loss is minimized, patients benefit from reduction of their exposure to the hazards of blood transfusion.

Complications of blood transfusion:

- ***Immune complications:*** Immune complications following blood transfusion are primarily due to sensitization of the recipient to donor red cells, white cells, platelets, or plasma proteins. Less commonly, the transfused cells or serum may mount an immune response against the recipient. Immune complications may be hemolytic or non-hemolytic.

1. *Hemolytic reactions;* Usually involve specific destruction of the transfused red blood cells by the recipient's antibodies. It may be acute intravascular hemolysis(usually due to ABO blood incompatibility), or delayed hemolytic reaction(extravascular- is generally mild and is caused by antibodies to non-D antigens of the Rh system).

2. *Non-hemolytic immune reactions*; Non-hemolytic immune reactions are due to sensitization of the recipient to the donor's white cells, platelets, or plasma proteins. These reactions may be febrile reactions, urticarial reactions, anaphylactic reactions, non-cardiogenic pulmonary edema, graft-versus-host disease, post-transfusion purpura, or immune suppression **(Lake & Moore, 1995).**

- ***Infectious complications:*** Many infectious agents may be transmitted via blood transfusion. Transmission of human immune-deficiency virus and hepatitis C virus has decreased over the years, and the estimated frequency of transmission is currently at 1/200,000- 1/2000,000 for hepatitis C virus. However new viruses have been discovered recently, such as hepatitis G virus, TT virus, and human herpes virus 8 associated with kaposi sarcoma. In addition, transmission of parasitic and bacterial diseases occurs sporadically and represents a substantial problem. Transmission of yet unknown viruses and the new variant Creutzfeld-Jakob disease via RBCs transfusion also appears possible and is a public concern **(Donat & Mattias, 2000).**

Methods to reduce blood loss in TKA

Blood loss and the need for blood transfusion depend on the technique and type of total knee arthroplasty. Revision and bilateral total knee arthroplasty were associated with more blood loss and

higher prevalence of blood transfusion **(Bould et al, 1998).** Blood loss in total knee arthroplasty is some-times profuse and often necessitates blood transfusion. The fibrinolytic system is activated during surgery, and the tourniquet augments this activation.

Tourniquets:

A pneumatic tourniquet placed proximal to a site of a peripheral procedure and inflated to occlude arterial flow eliminates blood loss during the operation. However significant losses still occur postoperatively, after the tourniquet is removed. Some surgeons routinely deflate the tourniquet before closing the wound to ligate or coagulate bleeding points. Whilst this may be of use in some procedures on the hand and other areas, when a hematoma may compromise the surgical result, it has been shown in one study not to reduce overall blood loss in total knee arthroplasty **(Lotke et al, 1992).** A prospective, randomized study done on 1999 by **Wakankar and his colleagues** to assess the influence of the use of tourniquet in total knee arthroplasty. There was no significant difference in the volume collected in the drains, and the incidence of deep venous thrombosis **(Wakankar et al., 1999).**

Thorpe, and his colleagues studied the effect of aprotinin in case of TKA, under tourniquet. They studied the effect of aprotinin on blood loss and subsequent blood transfusion in 17 patients undergoing knee replacement surgery. They concluded that, the role of aprotinin under tourniquet conditions is unclear **(Thorpe et al., 1994).**

A new method was tried for hemostasis during cementless TKA.

In brief, the implant was inserted after coating the exposed surface of the cancellous bone with fibrin glue Before removal of the tourniquet, after completion of the operation, 250mg of tranexamic acid in 50ml of physiological saline was injected into the joint cavity via the drain tube The drain tube was clamped for about 30 minutes after deflation of the tourniquet After removal of the clamp, standard negative pressure suction was applied This method was effective for achieving hemostasis after cementless TKA **(Akizuki et al., 1997).**

Fibrinolysis Inhibitors

The key substance in the fibrinolytic system is plasminogen which when activated releases the protease enzyme, plasmin which cleaves peptide bonds in fibrin, producing fibrinolysis **(Timothy et al., 1995).**

Fibrinolysis inhibitors include substances that reduce the fibrinolytic activity of blood and tissues. The objective of using them may be defined as follows: Inhibitors of fibrinolysis are indicated where there is an undesirable intensification of fibrinolysis, especially when accompanied by hemorrhages. Such conditions may develop on overdose or intensified reaction to administration of fibrinolytic agents; there may also be an important link in the pathogenesis of many hemorrhagic diseases and other pathologic conditions e.g. allergic phenomena, inflammation, rejections of transplanted organs and tissues **(Chazov, 1994).**

In their chemical structure and mechanism of action, the majority of fibrinolysis inhibitors can be classified into two main groups, synthetic inhibitors, and natural inhibitors.

(A)Synthetic Fibrinolysis Inhibitors:

Synthetic antifibrinolytic agents consist of synthetic amino and carbonic acids. To a greater degree, their action applies to plasmin activators. Among the synthetic antagonists of fibrinolytic agents, that are widely used in experimental and clinical medicine are E-aminocaproic acid(EACA),paramino-methyl-benzoic-acid(PAMBA) and trans-4amino-methyl-cyclohexane-1-carbonic acid. In spite of certain differences, their chemical structures have much in common **(Harrow et al,1990).**

(B)Natural Fibrinolysis Inhibitors:

This group includes inhibitors of animal and vegetative origin. For the most part, these substances inhibit the effect of the already activated and circulating plasmin (fibrinolysin) **(Lakin, 1992), e.g.; Aprotinin (trasylol)** is a naturally occurring protease inhibitor with inhibitory effects on human plasmin, trypsin, and tissue kallikrein **(Timothy et al, 1995).**

TRANEXAMIC ACID

Physical properties:

Tranexamic acid is a white crystalline powder. It is freely soluble in water and in glacial acetic acid, and practically insoluble in alcohol and ether A 5% solution in water has a pH of 6 5 to 8.0 (**Prod Info Cyclokapron (R), 1996).**

Synonyms to Tranexamic Acid :

- Acidum Tranexamicum,
- AMCA, and
- Trans-AMCA **(R P S G B, 1999).**

Presentation:

Tranexamic acid 500 mg tablets, and Tranexamic acid injection 100 mg/ml, which should be stored at room temperature **(R P S G B, 1999).**

Trade name:

- Cyclokapron,
- Cyclo-F,
- Anvitoff,
- Amcacid,
- Amchafibrin,Tranex,
- Tranexamic acid injection BP.

Multi-ingredient preparations:

- Caprofides Hemostatico,
- Transil**(R P S G B, 1999).**

Molecular formula:

$C_{8}H_{15}NO_{2}$.

Molecular weight:

157.2

Chemical name:

trans-4-(Aminomethyl)cyclohexanecarboxylic acid **(R P S G B, 1999).**

Phamacokinetics:

Tranexamic acid is absorbed from the gastrointestinal tract with plasma concentration occurring after about 3 hours. Tmexamic acid has a plasma elimination half-life of about 2 hours. It is excreted in urine mainly as unchanged drug, so should be given cautiously in patients with renal failure **(Reynold, 1998).**

Absorption and bioavailability

* *After* **intramuscular injection;** the bioavailability is 100% **(Puigdellivol et al., 1985).**

* *After* **oral administration;** the bioavailability is 33 to 35%. The systemic bioavailability of oral tranexamic acid is 33.4% in the fasting state and 35% in the presence of food **(Pilbrant et al., 1981).**

*After **topical (mouth rinse) application;** the systemic absorption of tranexamic acid mouth rinse is small. A 10 ml of 5% tranexamic acid mouth rinse leads to a peak plasma level less than 2 mcg/ml and very high saliva levels (200 mcg/ml) which remained in the therapeutic range for 2 hours **(Sidet-Pedersen, 1988).**

DISTRIBUTION:

The initial volume of distribution for tranexamic acid is

approximately 9 to 12 liters **(Puigdellivol et al., 1985).**

Other distribution sites include:

= *Aqueous humor*, 10% of plasma concentration .

#*Cerebrospinal fluid (CSF),* 10% of plasma concentration. Tranexamic acid crosses the blood brain barrier and suppresses fibrinolytic activity, primarily in the leptomeninges. The manufacturers report that the concentration of tranexamic acid in the cerebrospinal fluid is approximately one-tenth the concentration in plasma

#***Placenta;*** equivalent maternal plasma concentration. In the pregnant women, after an intravenous injection of 10 mg/kg, the concentration in cord blood is approximately 30 mg/l , the same as in maternal blood.

#***Semen;*** tranexamic acid passes into semen and inhibits fibrinolytic activity but has no influence on sperm migration.

#***Synovial fluid*** ; equivalent to plasma concentration. Tranexamic acid rapidly diffuses into joint fluid and Synovial membranes. The same concentration is reached in the joint fluid as in the serum and the half-life is approximately about 3 hours. (Verstraete; 1989).

#***Tissues;*** tranexamic acid demonstrates considerable antifibrinolytic activity in tissues (kidney, intestines, prostate). Trnexamic acid, at concentration of antifibrinolytic activity, persists in serum for up to 7 or 8 hours and in different tissues for approximately 17 hours **(Prod Information, 1996).**

Total protein binding;

Tranexamic acid is only minimally bound ,approximately 3%, to plasma proteins, primarily plasminogen, at therapeutic concentrations of 5 to 10 mcg/ml **(Reynolds, 1998).**

METABOLISM:

Less than 10% of the administered dose is metabolized in the body.

EXCRETION:

Kidney; renal clearance is 110 to 116 ml/min . Renal excretion is 39 to 95%. The elimination characteristics of tranexamic acid differ greatly depending upon whether given intravenously or by mouth. Following intravenous administration, approximately 95% of a dose are excreted unchanged in the urine. Other data have reported that 45% of a 10 mg/kg intravenous dose is excreted in the urine during the first 3 hours, with 90% being excreted over 24 hours. The overall renal clearance matches the overall plasma clearance at 110 to 116 ml/min. However, following an oral dose of 10 to 15 mg/kg; 1%, 13%; and 39% of the dose was recovered unchanged in the urine at 1, 3 , and 24 hours, respectively.

Breast milk; only minimal amount of the drug is excreted in breast milk (about 1% of peak plasma level) **(Verstraete, 1985)**

HALF-LIFE:

Elimination half-life is about 2 hours **(R P S G B, 1999).**

Place in therapy:

Tranexamic acid is a hemostatic agent used to treat or prevent excessive bleeding due to hyperfibrinolytic activity.

Mechanism Of Action:

Tranexamic acid exerts its antifibrinolytic effects primarily by

forming a reversible complex with a modified plasminogen and the associated conformational changes of this proenzyme. In fact, tranexamic acid saturates the lysine binding sites of human plasminogen, displacing plasminogen from the fibrin surface, which results in inhibition of fibrinolysis. Fibrinolysis is inhibited no matter how rapidly plasmin is formed, since plasmin is unable to bind to fibrinogen or fibrin monomers, precluding proteolytic action by the serene-histidine enzyme site **(Longstaff, 1994).**

Tranexamic acid also inhibits the proteolytic activity of plasmin via blockade of the lysine binding sites of plasmin, making inactivation by alpha-2-antiplasmin impossible. Recurrent or excessive bleeding can occur with defective fibrin formation or excessive rapid dissolution of fibrin; tranexamic acid can prevent the dissolution of hemostatic fibrin by stabilizing fibrin structures. The drug also increases collagen synthesis and tensile strength within granulation tissue, most likely by preserving the fibrin matrix.

Tranexamic acid and other antifibrinolytic agents cross the blood-brain barrier and counteract the increased fibrinolytic activity of cerebrospinal fluid. The drug has been used to prevent rebleeding of subarachnoid hemorrhage secondary to cerebral aneurysm by preserving the intact perianeurysmal clot formed within and around the wall of the aneurysm, to delay or prevent a second rupture **(Longstaff, 1994).** In summary, tranexamic acid produces antifibrinolytic activity via complex interactions with plasminogen, displacing plasminogen from the fibrin surface.

Therapeutic uses:

1) ***Arthroplasty;*** Tranexamic acid significantly reduced the blood loss in patients undergoing total knee arthroplasty with the use of a pneumatic tourniquet. No increase was observed in the risk of thromboembolic complication **(Hippala et al., 1997).** Intravenous administration of tranexamic acid started before total hip replacement decreased the perioperative bleeding to 65% of the control group value (**Gustav et al, 2000**)
2) ***Cardiac surgery:*** Reduced perioperative blood loss in most studies in adults and children undergoing cardiac surgery and cardiopulmonary bypass. It is recommended that to use tranexamic acid prior to initiating cardiopulmonary bypass in patients at high risk for excessive bleeding related to cardiac surgery. The benefits of post-bypass administration are less evident **(Brown et al, 1997).**
3) ***Tonsillectomy:*** Tranexamic acid reduced blooding during and after tonsillectomy, which is the most common complication of tonsillectomy **(Product Information, 1998).**
4) ***Subarachnoid hemorrhage:*** Not recommended due to association with ischaemic complications, but it may have some benefit combined with nimodipine **(Stroobandt et al, 1998).**
5) ***Angioneurotic edema:*** Tranexamic acid was proved to reduce the frequency of the attacks in patients with nonhereditary **(Sheffer et al., 1999),** and hereditary Angioneurotic edema **(Crosher, 1987).**
6) ***Dental procedures for anticoagulated patients:*** Tranexamic acid

mouthwash useful in the prevention of bleeding after oral surgery in patients on anticoagulant therapy **(Ramstrom et al, 1993).**

7) ***Cancer-associated hemorrhage:*** Suppressed capillary ooze associated with cancerous tumors **(Dean & Tuffin, 1997)(Seto & Dunlap, 1996).**

8) ***Uterine(Cervical)conization:*** tranexamic acid reduces postoperative hemorrhage after cervical conization **(Rybo, 1991).**

9) ***Colitis:*** A significant reduction in rectal bleeding due to ulcerative colitis was reported following tranexamic acid 1.5 gm orally 3 times daily for three weeks. Tranexamic acid enema was used in ulcerative colitis, and pseudomembranous colitis to reduce rectal bleeding (Kondo et al, 1981).

10) ***Congenital diaphragmatic hernia:*** Reduced bleeding and transfusion requirements in patients requiring extracorporeal membrane oxygenation **(Product Information, 1998).**

11) ***Gastrointestinal hemorrhage:*** Reduced transfusion requirements and/or mortality in patients with upper gastrointestinal hemorrhage **(McCormick et al, 1998).**

12) ***Liver transplantation:*** Intraoperative low-dose infusion may decrease fibrinolysis but not transfusion requirements **(Boylan et al., 1996).**

13) ***Dental extraction in hemophilic patients:*** To prevent hemorrhage and reduce the need for replacement therapy. Tranexamic acid mouthwash preferred over systemic therapy for control of bleeding

after dental procedures in hemophilic **(Sindet-pedersen et al, 1988).**

14) *Cystic fibrosis:* Tranexamic acid was a useful adjunct to bronchial artery embolization in preventing the recurrence of hemoptysis **(Wong et al., 1996).**

15) *Epistaxis:* oral dose of 1.5 gm times per day effective for treatment of recurrent epistaxis in a controlled study **(Product Information, 1998).**

16) ***Malignant mesothelioma:*** Malignant mesothelioma with bleeding pleural effusion was successfully treated with oral tranexamic acid 1 gm four times daily in addition to 2 daily doses of tranexamic acid 5 gm given intrapleurally. Short-term management effectively controlled bleeding and transfusion requirements were reduced **(De Boer et al., 1991).**

17) ***Ophthalmology:*** Tranexamic acid has been useful in the treatment of hyphema and in several ophthalmic surgery procedures. Two studies demonstrated benefits in reducing corneal edema after cataract surgery and trabeculectomy surgery **(Olsen et al, 1980).**

18) ***Prostatectomy:*** Although tranexamic acid, one gm orally ,three times daily for several weeks has been effective in reducing the frequency of secondary hemorrhage following prostatectomy **(Miller et al., 1980).** But it is not recommended for routine use after prostatectomy due to increased incidence of intravesicular blood clot formation **(Product Information, 1998).**

19) ***Menorrhagia:*** Tranexamic acids is effective for treatment of menorrhagia and menorrhagia associated with intrauterine devices (IUD) **(Ong et al, 1998).**

20) ***Ovarian carcinoma:*** Malignant ovarian tumors possess both coagulative and fibrinolytic properties High amounts of fibrinogen-fibrin degradation products have been observed in serum and ascetic fluid of patients with ovarian tumors, and tranexamic acid showed some efficacy in arresting tumor growth.

21) ***Post-partum hemorrhage:*** Tranexamic acid 1 gm administered intravenously 4 hours after surgery and repeated after 4 hours was used successfully to control postpartum hemorrhage in placenta previa and placenta accreta. **(Hagen & Web, 1996).**

22) ***Abruptio placenta:*** Reduced perinatal mortality **(Svanberg et al., 1999).**

PRECAUTIONS

Tranexamic acid should not be given in patients with active intravescular clotting because of the risk of thrombosis. Tranexamic acid should be given very cautiously in the following conditions:

- Cardiovascular disease
- Cerebrovascular diseases
- Concomitant antifibrinolytic therapy
- Concomitant therapy with estrogen and thrombolytics
- Renal impairment
- transurethral prostatectomy (potential for intravesicular clotting).

ADVERSE REACTIONS;

1. *Hematological effects:*

* Thrombocytopenia, has been rarely reported.

* Abnormal bleeding times

* Coagulation defects(or disorders), have been described , although rarely **(R P S G B, 1999).**

2. ***Thromboebolism:*** A retrospective review of medical records of pregnant women with various bleeding disorders failed to demonstrate a relationship between the administration of tranexamic acid and an increased risk of Thromboembolism **(Lindof, et al., 1993).**

Systemic thromboembolic complications have been reported with tranexamic acid, which include Thromboembolism, myocardial infarction, and pulmonary embolism **(Woo et al., 1989).**

3. ***Cardiovascular effects :*** Hypotension has been reported occasionally with the use of tranexamic acid, primarily when intravenous injection of the drug is done rapidly (administered at a rate greater than one ml/min.).

4. ***Central nervous system :*** The most serious adverse effects of tranexamic acid are cerebral ischaemia and infarction, which have occurred during use of the drug to prevent re-bleeding in subarachnoid hemorrhage. Other side effects included headache and psychotic problems **(Van, 1992).**

Hydrocephalus has also been recorded, since tranexamic acid inhibits fibrinolysis, retained clots around the arachnoid villi may

induce scarring and decrease cerebrospinal fluid(CSF) absorption, predisposing to the development of hydrocephalus, which may require CSF drainage

5. ***Gastrointestinal tract :*** Gastrointestinal disturbances *(NAUSEA, VOMITING, and DIARRHEA)* are the primary side effects of tranexamic acid therapy; these symptoms will improve if the tranexamic acid dosage is reduced **(Vermeulen et al., 1984).** Nausea and diarrhea appear to be more common with oral therapy as opposed to intravenous therapy. Abdominal pain has also been reported with oral therapy (Munch & Week, 1985).

6. ***Ocular:*** Central venous stasis retinopathy was reported in women receiving tranexamic acid for sever menorrhagia **(Snir et al., 1990).**

7. ***Teratogenicity :*** Limited data using tranexamic acid during pregnancy have revealed no harmful effects on the fetus, and it is considered as category B1 by the Australian Drug Evaluation Committee's **(ADEC, 1996).**

8. ***skin :*** Purpuric skin rashes have been observed with aminocaproic acid treatment, but not with tranexamic acid **(Kavanagh, 1993).**

Comparative Efficacy And Evaluation With Other Therapeutic Agents:

* *Aminocparoic Acid :*

High-dose tranexamic acid and epsilon aminocaproic acid, administered prophylactically during cardiopulmonary bypass, were equally effective in reducing transfusion requirements in patients

undergoing first-time, coronary artery bypass grafting with cardiopulmonary bypass **(Hardy et al, 1998).**

Tranexamic acid may have more sustained antifibrinolytic effects and is 6 to 10 times more potent than aminocaproic acid in fibrinolytic activity. IN addition, tranexamic acid has greater and more sustained antifibrinolytic activity in tissues than aminocaproic acid, and appears to have the same order of acute and chronic toxicity **(Verstraete, 1985).**

Due to a high incidence of ischaemic complications, tranexamic acid is not recommended in patients with subarachanoid hemorrhage **(Vermeulen et al, 1984).**

** Aprotinin*

Tranexamic acid and aprotinin were equally effective in reducing postoperative blood loss, frequency of transfusion, and volume of blood products transfused in 150 patients undergoing primary coronary artery bypass grafting **(Blauhut et al, 1994)**. Both agents were superior in producing these outcomes when compared with 30 placebo-treated patients receiving otherwise similar management **(Mongan et al, 1998).** Tranexamic acid and aprotinin reduce blood loss in orthopedic surgeries **(Capdevila et al, 1998)**

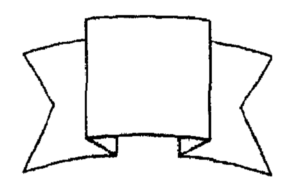
** Cimetidine*

Tranexamic acid was reported at least as effective as Cimetidine in reducing mortality in acute upper gastrointestinal tract bleeding.

** Diclofenac*

The superiority of tranexamic acid over diclofenac was reported in the

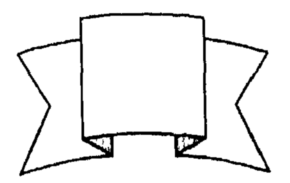
treatment of menorrhagia in women with an intrauterine device and heavy menstrual bleeding. Although tranexamic acid was more effective than diclofenac, diclofenac is recommended over tranexamic acid for the initial treatment of menorrhagia due to the lower incidence of side effects observed. Tranexamic acid could be considered if diclofenac is ineffective **(Ylikorkala and Viinikka, 1983).**



Aim of the Work

AIM OF THE WORK

The aim of this study was to evaluate clinically the effect of tranexamic acid (cyclokapron), on postoperative blood loss, the need for blood transfusion, the changes in coagulation profile, and complications associated with total knee arthroplasty with the use of tourniquet



Patients and Methods

PATIENTS & METHODS

This prospective, randomized double blind, controlled study was done, after getting consent from the patients. The study included Sixty patients of both sexes, of ASA physical status I, or II undergoing total knee arthroplasty with use of a tourniquet. The patients were randomly (using blinded envelopes) allocated into one of two groups.

Group one(Test Group):

This group included 30 patients. Patients of this group received, 15 mg/kg body weight, I.V. bolus dose of tranexamic acid (TA) 3-5 minutes before deflation of the pneumatic tourniquet.

Group two(Control Group):

This group included 30 patients. Patients of this group received an equal volume of placebo (normal saline) I.V. 3-5 minutes before deflation of the tourniquet.

Way of randomization

Randomization was carried out by an anesthesiologist not involved in the operation, using a ticket drawn from an envelope containing an equal number of tranexamic acid and placebo tickets. The operating team was unaware of the contents of the solution administered.

All patients were subjected to the following:

Medical History;

Full history was taken from all patients, stressing on family or past history suggestive of bleeding diathesis. Inquiry was also done to exclude administration of drugs that affect hemostasis and bleeding profile e.g ; warfarin.

Thorough Clinical Examination,

Thorough clinical examination was done to all patients with special stress on any signs suggestive of hemostatic disorders or bleeding tendency.

Patient Exclusion

All patients with history of bleeding diathesis, with signs of spontaneous bleeding tendency on clinical examination, or having abnormal results of laboratory tests for hemostasis that have been done before the operation were excluded from study.

Patient Instructions,

Patients were requested to stop medications containing acetyl salicylic acid one week before the operation.

Statistical Methods

The statistical tests used in result analysis were Chi-square test, and Student "t" test

Anesthesia

- *Pre-medication:* 1-3 mg of lorazepam (ativan) 2 hours preoperatively.
- *Induction of anesthesia:* Sleeping dose of thiopentone (3-5 mg/kg) , 1-3 ug/kg of fentanyl, non-depolarizing muscle relaxant (atracurium{0.5 mg/kg} or vecuronium{0.01 mg/kg}).
- *maintenance of anesthesia:* Anesthesia was maintained using Nitrous oxide in oxygen (1:1), with either halothane or isoflurane. N.B.: All patients were given 5000 i.u. of heparin subcutaneeously as a prophylaxis against deep venous thrombosis, starting the night before surgery, and repeated twice daily until patients sufficiently mobilize.

Laboratory Tests,

♦ Twenty-four hours before the operation:

Hemoglobin concentration (Hb(gm/l)), hematocrit value (Hct), platelet count, bleeding time (BT), activated partial thromboplastin time (APPT), Prothrombin time (PT), fibrinogen level, and fibrin degradation product (FDPs) were measured for all patients.

♦ *Eight hours after surgery:*

Hemoglobin concentration, hematocrit value, platelet count, bleeding time, PT, APTT, fibrinogen level, and FDPs were measured for all patients 8 hours after the operation.

♦ *On the first and second day after the operation:*

Hemoglobin concentration, hematocrit value, platelet count, bleeding

time , PT, APTT, fibrinogen level, and FDPs were measured for all patients on the first and second postoperative day.

Fluid therapy

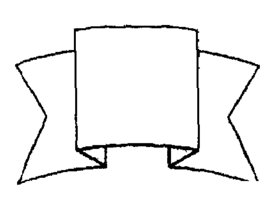
Lactated ringer's solution and hydroxyethyl starch was used as the replacement fluids (5:1). The total volume of all I.V. fluids was recorded from induction to the second morning after operation. The number of transfused units of blood during the hospital stay was also recorded.

Assessment of blood loss and need for blood transfusion

During operation, blood loss was assessed, by measuring the weight change of surgical swabs, and the volume in the suction reservoir. In the recovery room and the surgical ward, the contents of the drain reservoir were measured and recorded. If the hemoglobin concentration was less than 100 gm/liter, concentrated red cells were given.

Detection of thromboembolic complications

Ultrasonic screening was used for early detection of deep venous thrombosis in both legs. Ultrasonic screening was performed on day 3 and day 10 postoperatively by an experienced radiologist with real-time B-mode ultrasonography.



Results

Results

Patient characteristics

Table 1 shows comparison between the two studied groups (control and test groups), as regard age, weight, operative duration, and duration of tourniquet application. There was no statistically significant difference between the two groups in any of these values.

Table (1) age, weight, and duration of operation, and tourniquet inflation

	Test group	Control group
Age (year)	59.2 (9.0)	60.2 (7.7)
Weight (kg)	79.4 (9.5)	83.1 (9.2)
Duration of operation (min)	137.8 (7.8)	137.2 (11.0)
Duration of tourniquet inflation (min)	118.5 (7.9)	115.0 (8.3)

Data are presented as mean ± (SD)

Perioperative hemoglobin (Hb)

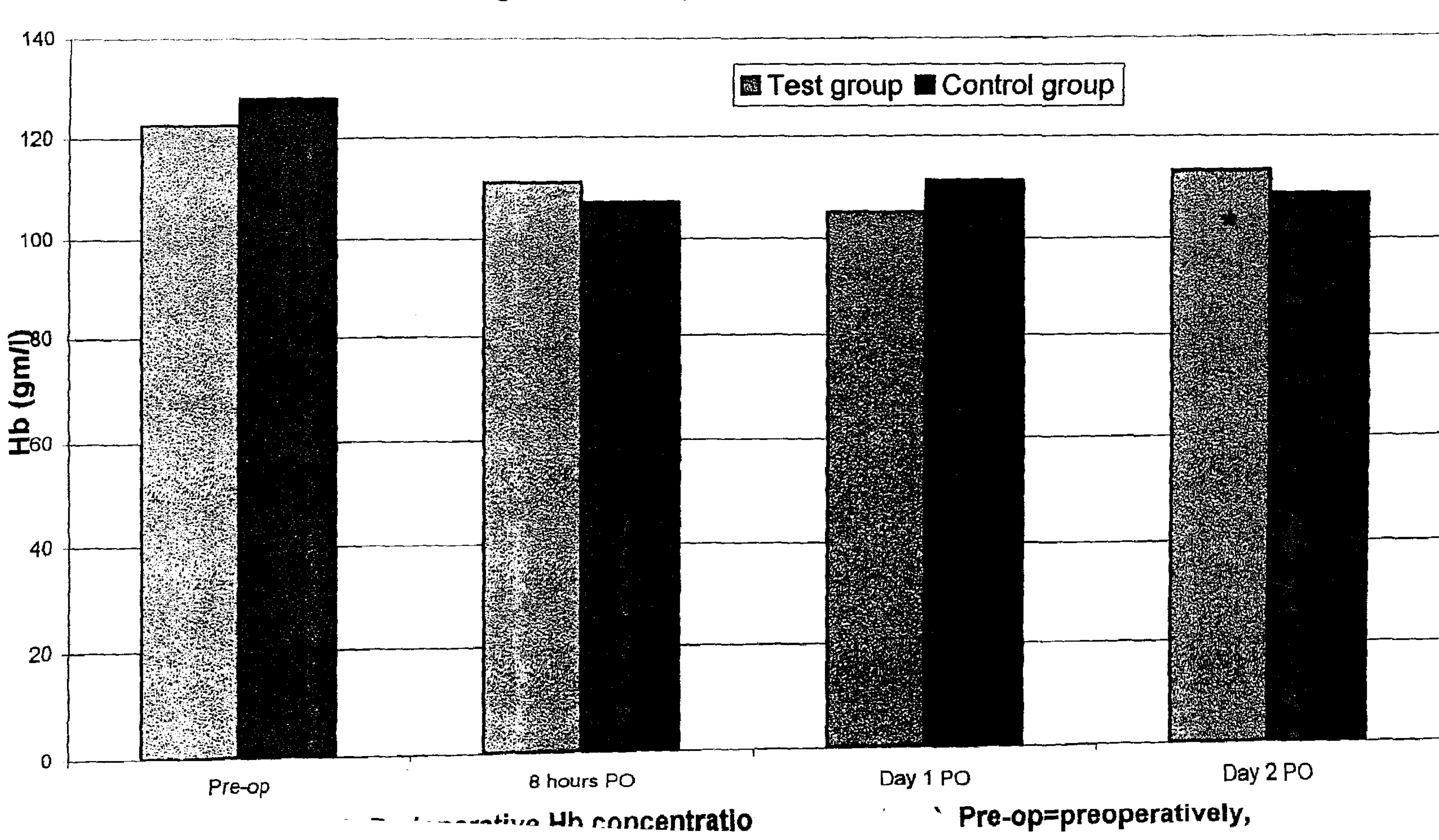
Table 2 and figure 1 show that, there was no statistical significant difference between test and control groups as regard, hemoglobin concentration done preoperatively There was statistically significant difference between both groups as regard hemoglobin concentration done two days postoperatively.

Table 2: Hemoglobin concentration (Hb) in gm/l

	Test group	Control group
Pre-op	127.8 (10.6)	122.5 (15.7)
8 hours PO	111.2 (10.5)	107.3 (11.5)
Day 1 PO	111.3 (9.2)	105.3 (8.6)
Day 2 PO	113.2 (9.3)*	108.9 (9.0)*

Data are presented as mean ±(SD)
Pre-op=laboratory analysis done before surgery, PO=postoperatively
Significant differences between the groups are described with * $P< 0.05$

Figure 1: Hemoglobin concentration (Hb)



Hb concentratio Pre-op=preoperatively,

Perioperative hematocrit

Table 3 shows that, there was no statistically significant difference between test and control groups as regard, hematocrit value done preoperatively, eight hours, and first day postoperatively. There was statistical significant difference between both groups as regard, Hct value in second postoperative day.

Table 3: Hematocrit value (%)

	Test group	Control group
Pre-op	36.7 (3.6)	36.2 (4.5)
8 hours PO	33.2 (3.6)	32.0 (3.7)
Day 1 PO	31.9 (2.9)	30.4 (3.4)
Day 2 PO	33.9 (3.1)*	30.5 (3.2)*

Data are presented as mean ±(SD)
Pre-op=laboratory analysis done before surgery, PO=postoperatively
Significant differences between the groups are described with * $P< 0.05$

Perioperative platelet count

Table 4 shows that, there was no statistically significant difference between test and control groups as regard, platelet count in either preoperatively or postoperatively at any measuring time.

Table 4: Platelet count (10^9/l)

	Test group	Control group
Pre-op	252 (79)	242 (52)
8 hours PO	248 (76)	228 (87)
Day 1 PO	240 (78)	242 (83)
Day 2 PO	243 (74)	243 (81)

Data are presented as mean ± (SD)
Pre-op=laboratory analysis done before surgery, PO=postoperatively

Perioperative bleeding time (BT)

Table 5 shows that there was no statistical significant difference between both groups as regard, bleeding time in preoperative or any postoperative measuring times

Table 5: Bleeding time (BT) in minutes

	Test group	Control group
Pre-op	6.5 (1.4)	5.9 (2.0)
8 hours PO	6.1 (1.3)	6.0 (1.4)
Day 1 PO	6.3 (2.1)	6.8 (2.5)
Day 2 PO	7.1 (2.3)	7.3 (1.5)

Data are presented as mean ± (SD)
Pre-op=laboratory analysis done before surgery, PO=postoperatively

Perioperative prothrombin time (PT)

Table 6 shows the statistical difference between test and control groups as regards, Prothrombin time. There was no statistically significant difference preoperatively, or eight hours postoperatively. There was statistically significant difference between both groups as regards, PT done first and second postoperative days.

Table 6: Prothombin Time (PT) in seconds

	Test group	Control group
Pre-op	13.1 (0.7)	13.2 (1.3)
8 hours PO	14.1 (1.04)	13.6 (1.09)
Day 1 PO	13.4 (1.07)*	14.5 (1.1)*
Day 2 PO	13.4 (1.05)*	14.4 (1.05)*

Data are presented as mean ± (SD)
Pre-op=laboratory analysis done before surgery, PO=postoperatively
Significant differences between the groups are described with * $P < 0.05$

Perioerative Activated Partial Thomboplastin Time (APTT)

Table 7 shows comparison between test and control groups as regard, Activated Partial Thromboplastin Time (APTT). There was no statistical significant difference between both groups as regard APTT done preoperatively or eight hours postoperatively. But there was statistically significant difference between the two groups in first and second postoperative days.

Table 7: Activated Partial Thomboplastin Time (APTT) in seconds

	Test group	Control group
Pre-op	32.8 (3.6)	33.9 (3.5)
8 hours PO	36.9 (4.7)	35.9 (3.4)
Day 1 PO	35.5 (3.5)*	37.2 (3.8)*
Day 2 PO	35.3 (3.2)*	37.7 (3.5)*

Data are presented as mean ± (SD)
Pre-op=laboratory analysis done before surgery, PO=postoperatively
Significant differences between the groups are described with * P< 0 05

Perioperative fibrinogen level

Table 8 and figure 2 show that there was no statistically significant difference in fibrinogen level between test and control groups preoperatively or eight hours postoperatively. While, the statistical difference was significant in first postoperative day, and highly significant in second postoperative day.

Table 8: Fibrinogen level in both groups in gm/l

	Test group	Control group
Pre-op	3.1 (0.4)	3.2 (0.2)
8 hours PO	3.2 (0.6)	3.2 (0.4)
Day 1 PO	2.3 (0.6)*	2.0 (0.5)*
Day 2 PO	2.5 (0.5)†	2.0 (0.7)†

Data are presented as mean ± (SD)
Pre-op=laboratory analysis done before surgery, PO=postoperatively
Significant differences between the groups are described with * P< 0.05, † P<0 01

Figure 2 : Fibrinogen level

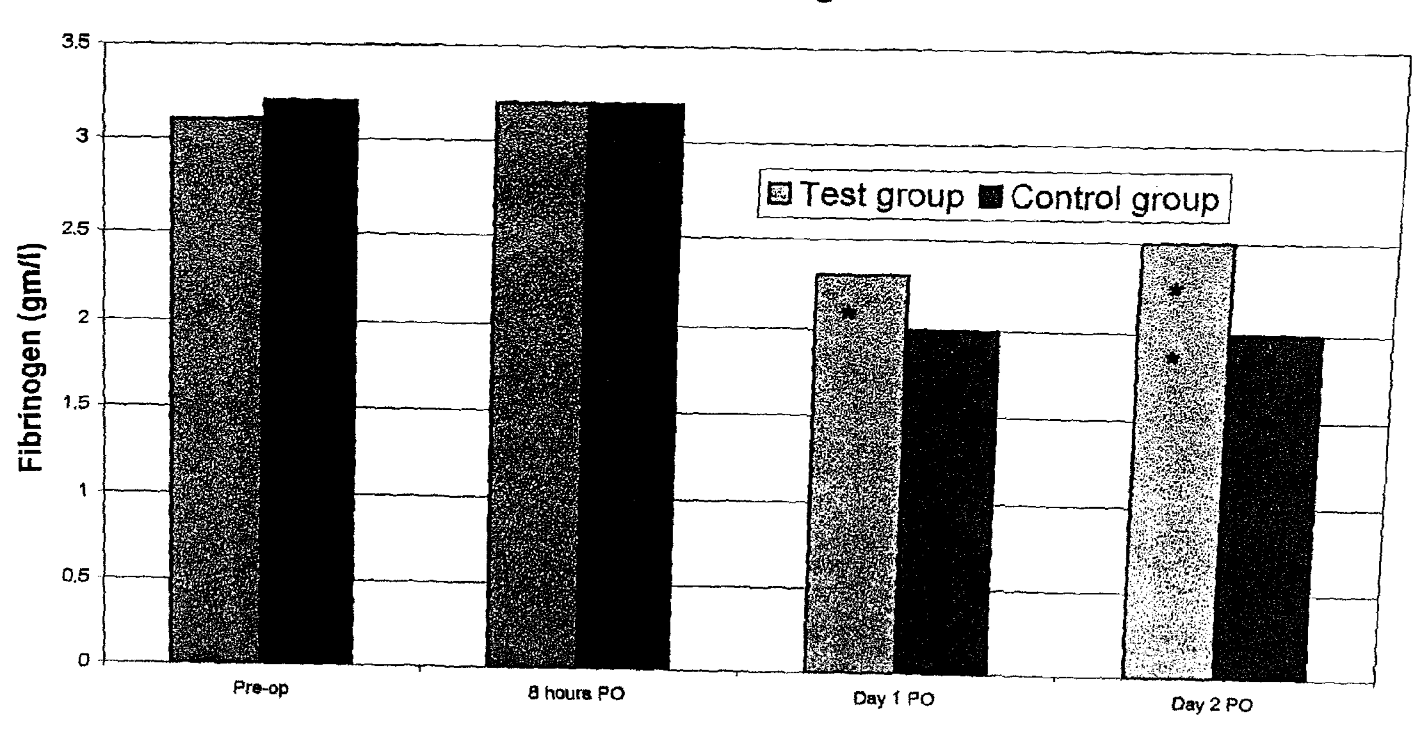


Figure 2: Perioperative fibrinogen level . Pre-op=preoperatively, PO=postoperatively,*P<0.05, **P<0.01

Perioperative Fibrin Degradation Products (FDPs) in both groups

Table 9 and figure 3 show that there was a highly significant statistical difference between test and control groups as regard, fibrin degradation products measured at all postoperative times.

Table 9: Fibrin Degradation Products (FDPs) in both groups in ug/ml

	Test group	Control group
Pre-op	0.27 (0.06)	0.23 (0.04)
8 hours PO	1.03 (0.04) ‡	1.89 (0.3) ‡
Day 1 PO	1.1 (0.2)	1.4 (0.2)
Day 2 PO	0.8 (0.2) †	1.1 (0.2) †

Data are presented as mean (SD)
Pre-op=laboratory analysis done before surgery, P.O.=postoperatively
Significant differences between the groups are described with †$P<0.01$, ‡$P<0.001$

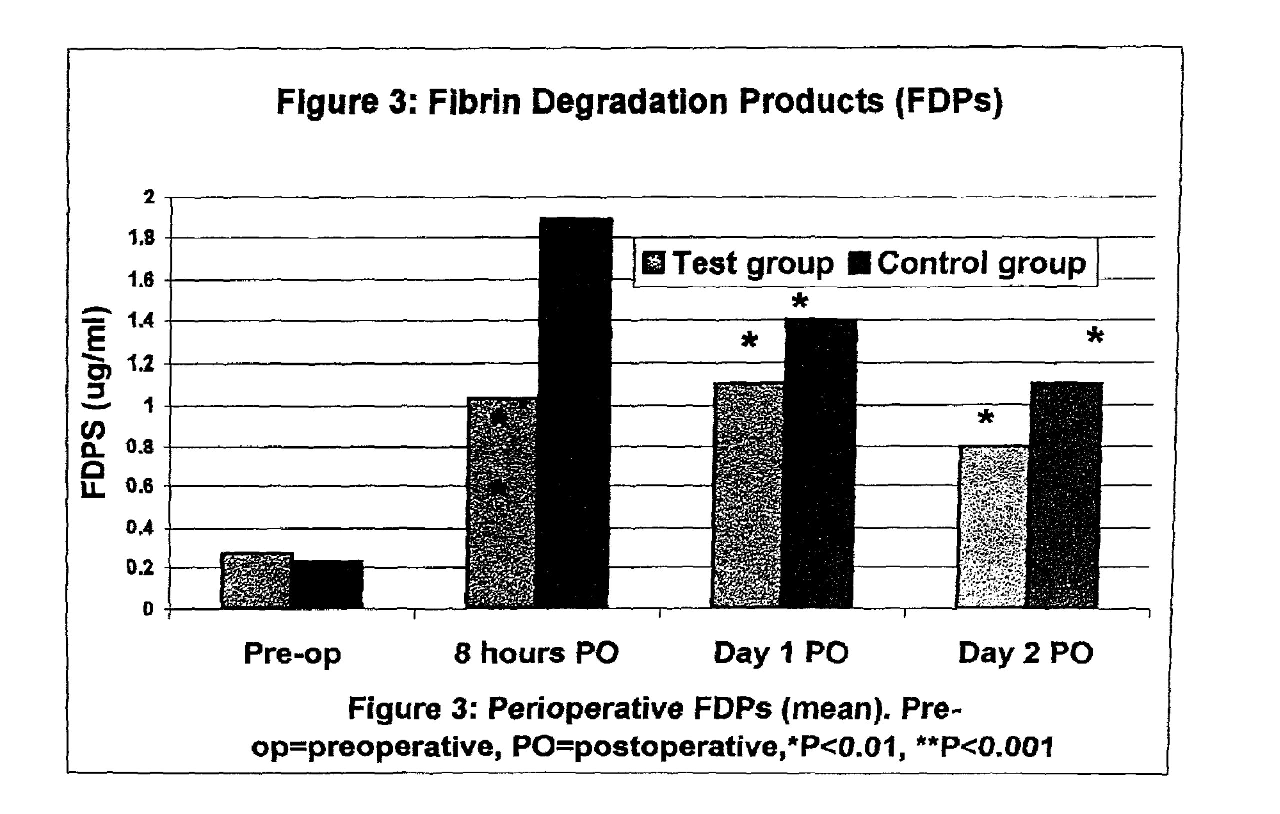


Figure 3: *Perioperative FDPs (mean). Pre-op=preoperative, PO=postoperative,*P<0.01, **P<0.001*

Blood Loss

Table 10 and figure 4 show the blood loss in both test and control patients. Mean blood loss in the day of surgery was 367.2 +/- 125 ml in test group, and 687.9 +/- 267.8 ml in control group. Statistical difference was highly significant ($p<0.001$). On the first day postoperatively, test patients lost a mean of 213.1 +/- 106.6 ml of blood, while control patients lost a mean of 334.3 +/- 214.3 ml; the difference was statistically highly significant ($p<0.01$). Blood loss was also significantly less in test patients than in control patients on the second day postoperatively. Mean blood loss in the former was 28.1 +/- 24.8 ml, and 57.2 +/- 125 ml in the latter ($p<0.05$). Mean total volume of blood loss after the operation was 608.5 +/- 160.2 ml in test group, and 1079.41 +/- 356.5 ml in the control group. The difference was statistically highly significant ($p<0.001$).

Blood Transfusion

Ten patients from the test group (n=30) needed blood transfusion, as compared to twenty-three patients from the control group (n=30) who needed blood transfusion.

Table 11 shows that, the mean volume of blood transfused was 250 +/- 388.3 ml for test patients, and 683.3 +/-444.9 ml for control patients, the difference was highly significant (**figure 5**).

Table 10: Blood loss after operation in ml

	Test group	Control group
Day of surgery	367.2 (125) ‡	687.9(267.8) ‡
Day 1 PO	213.1(106.6) †	334.3(214.3) †
Day 2 PO	28.1(24.8)*	57.1(56.1)*
Day 2 PO	608.5(160.2) ‡	1079.4(356.5) ‡

Data are presented as mean ±(SD) , PO=postoperatively
Significant differences between the groups are described with * $P<0.05$, †$P<0.01$, ‡$P<0.001$

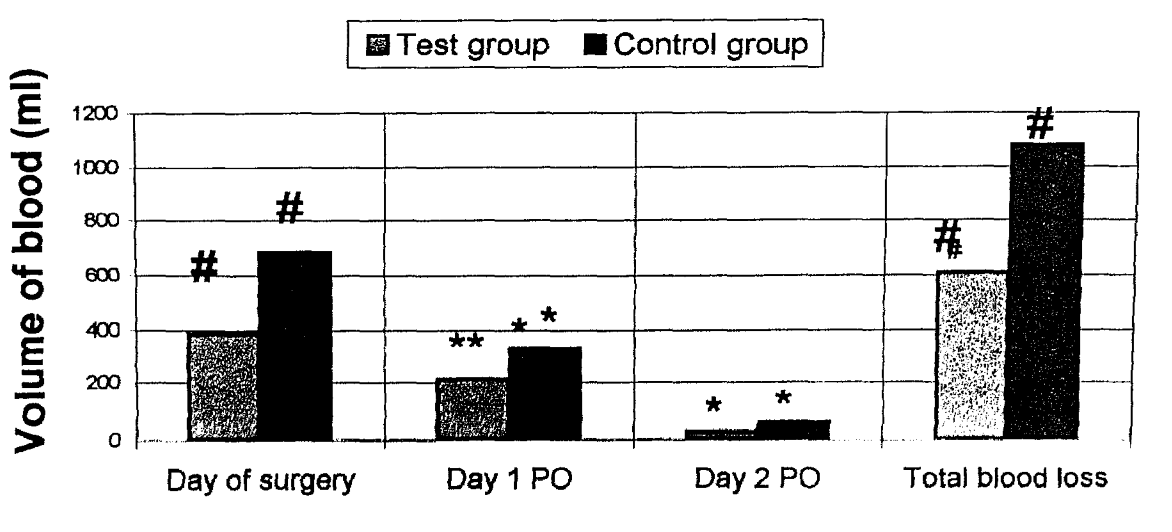


Figure 4:postoperative blood loss (mean). PO=postoperative,*P<0.05, **P<0.01, #P<0.001

Figure 5: Blood transfusion

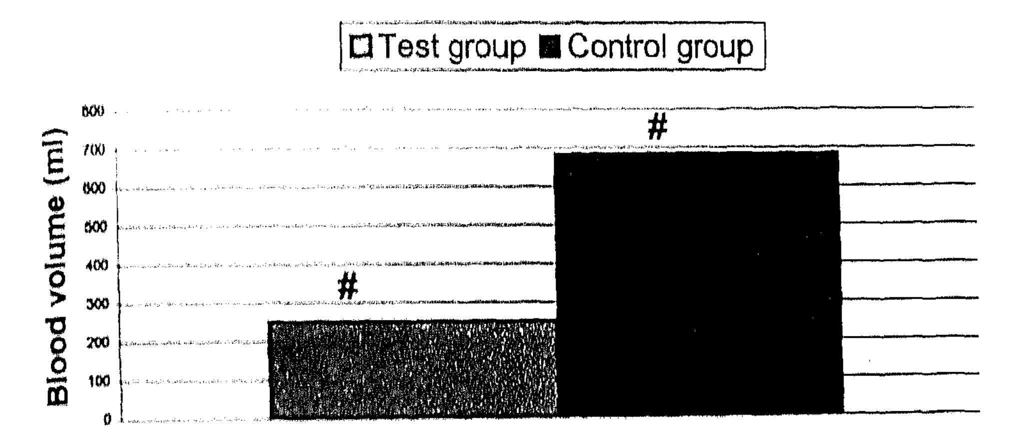


Figure 5: Postoperative blood loss (mean). #P<0.01

Fluid Transfusion

Patients in test group required a mean of 2509 +/- 345 ml of ringers solution, and a mean of 419 +/- 390 ml of hydroxyethyl starch as volume replacement. While, patients in control group required a mean of 2900 +/- 308 ml of ringers solution, and a mean of 750 +/- 339 ml of hydoxyethyl starch **(Figures 6).**

Table (11) Fluid transfusion in ml

	Test group	Control group
Blood (ml)	250.0 (388.4)†	683.3 (444.9) †
Ringer (ml)	2509 (345)*	2900 (508)*
HES (ml)	419 (390)*	750 (339)*

Data are presented as mean (SD)
Significant differences between the groups are described with * P<0.05, †P<0.01.

Postoperative complications:

Non of our patients of either group manifested thromboembolic or other complications.

Figure 6: Fluid transfusion

Ringer HES

Volume in ml

3500
3000
2500
2000
1500
1000
500
0

Test group

Control group

Discussion

Discussion

Our study shows that patients who were given tranexamic acid (TA) [TA group] had significantly less total blood loss compared with patients who received placebo (placebo group) both in the operative day and the following 2 days postoperatively

Our results confirm the rational effect of TA on reduction of blood loss following total knee arthroplasty (TKA). The single-dose therapy of TA (15 mg/kg) reduced the mean blood loss by 320 ml in the day of surgery (P<0 001), 121ml in the first day postoperatively (P<0.01), 29 ml in the second postoperative day (P<0 05). The mean total postoperative blood loss was less by 470 ml as compared to placebo group (P<0.001). Additionally, blood transfusion requirements were also less in the test group. The volume of transfused blood was significantly reduced by about 433 ml (P<0.001), and the number of patients who needed blood transfusion by more than 50% compared to the placebo group.

Our findings parallel those of similar studies done on patients who were undergoing TKA, using TA in different dosing regimens. **In 1995, Benoni and his colleagues** conducted a retrospective study. They used TA in a single dose of 15 mg/kg before deflation of the tourniquet, for 70 patients who were operated upon for TKA, and 109 patients who underwent total knee arthroplasty before this treatment was introduced, served as control group. Multiple regression analysis showed that the mean total postoperative blood loss was 340 ml less in

treated patients compared with control group.

In the previous study, the magnitude of reduction of blood loss after total knee arthroplasty was slightly less than our value (470 versus 340), but this may be due to the retrospective nature of this study.

Another study, using single dose of TA, has been conducted by **Hiippala et al (1995).** Twenty-nine patients were allocated randomly to receive either TA (15 mg/kg), or an equal volume of placebo a few minutes before deflation of the tourniquet The total postoperative blood loss reduced from 1549 +/- 574 ml (in the control group) to 847 +/- 356 ml (in the test group) (P<0.01). During the hospital stay the treatment group received 1.5 +/- 1.3 units of blood compared with 3.3 +/- 1.8 units in the control group (P<0.005). These results are comparable to our results.

There are multiple different studies used TA in multiple doses during and after TKA. **In 1996, Benoni and Fredin** investigated the effect of tranexamic acid, on blood loss and blood transfusion in knee arthroplasty. A dose of 10-mg/kg body-weight of either tranexamic acid or placebo was given intravenously shortly before the release of the tourniquet, and repeated three hours later. The mean total blood loss was 630 +/- 280 ml in the tranexamic acid group as against 1410 +/- 480 ml in the placebo group (P<0.0001). Both the number of patients received blood transfusion and the number of blood units

transfused were reduced to one-third in the treatment group, and mean postoperative Hb concentrations were significantly higher after prophylaxis

In the previous study, the reduction of blood loss was more than that in our study The prolonged postoperative high serum level of TA, owing to second dose injection of TA may explain this

Hiippala and his associates (1997) have done another study on seventy-five patients scheduled for 77 total knee arthroplasty (TKAs). They used tranexamic acid in three successive doses. The patients were randomized to receive either TA (n = 39) or equal volume of normal saline (NS, n = 38). Before deflation of the tourniquet, 15 mg/kg of TA was given intravenously followed by two 10-mg/kg additional doses. Perioperative blood loss was measured. The number of transfusions given during hospitalization was registered. Total blood loss was 689 +/- 289 ml in the TA group and 1509 +/- 643 ml in the NS group (P<0.0001). The mean number of transfused red cell units in the TA group was 1.0 +/- 1.2 compared to 3.1 +/- 1.6 in the NS group (P<0.0001). Twelve patients in the TA group and thirty four patients in the NS group were given blood transfusion. Two patients in the TA group and three in the NS group had a deep venous thrombosis, including a fatal case of pulmonary embolism in the NS group. They concluded that short-term TA therapy significantly reduces TKA-associated blood loss and transfusion requirements without increasing thromboembolic complications.

In 1999, Benoni has done a prospective, double blind, placebo-controlled study, using TA in a single dose 15 mg/kg He has found that TA reduced blood loss by half, and the need for blood transfusion by two thirds

In 1999 Jansen and his colleagues have done a randomized, double blind, placebo-controlled study on patients undergoing total knee arthroplasty. Tranexamic acid 15 mg/kg (n=21), or an equivalent volume of normal saline (n=21) was given 30 minutes before deflation of the tourniquet and subsequently every 8 hours after surgery for 3 days. Total blood loss in the tranexamic acid group was 678 +/-352 ml compared with 1419 +/- 607 ml in the control group ($P<0.001$), and occurred primarily during the first 24 hours after surgery. Thirteen patients received packed red blood cells in the control group compared with two patients in the tranexamic acid group ($P<0.001$). The previous study showed that repeating tranexamic acid injection more than twice cause no more reduction of blood loss. And these findings may be explained by the limited postoperative enhancement of fibrinolytic activity to the early postoperative period.

In our study, during the perioperative period up to second day postoperatively, coagulative and fibrinolytic screening was done. Platelet count, and bleeding time did not show any significant statistical difference between the two studied groups. There was statistical significant difference between the two groups as regard, PT,

and APTT at first and second postoperative days (may be due to the anticoagulant effect of the increased fibrin degradation products) **(Hunt, 1995).** There was markedly less fibrinolytic activity in the tranexamic acid group early postoperatively and up to second day postoperatively, as shown by the highly significant statistical difference between groups as regards, fibrinogen level and FDPs. This less fibrinolytic activity in tranexamic acid group is the anticipated mechanism of action of tranexamic acid to reduce both blood loss and blood transfusion requirements.

In 1997, Akazuki and his colleagues have tried a new method for hemostasis during cementless TKA. In brief, the implant was inserted after coating the exposed surface of the cancellous bone with fibrin glue. Before removal of the tourniquet, and after completion of the operation, 250mg of tranexamic acid in 50ml of physiological saline was injected into the joint cavity via the drain tube. The drain tube was clamped for about 30 minutes after deflation of the tourniquet. After removal of the clamp, standard negative pressure suction was applied. The mean total amount of blood loss during and after the operation was 235+/-178ml in unilateral TKA patients and 402+/-208ml in bilateral TKA patients. No patients required blood transfusion post-operatively. Comparison of these results with mean blood loss and blood transfusion after total knee arthroplasty with cement, shows that, this method was effective for achieving hemostasis after cementless TKA.

A study done on 1997 **by Benoni and his colleagues**, they investigated the effect of tranexamic acid on local and plasma fibrinolysis during total knee arthroplasty, in order to find out (1) Whether an increased fibrinolysis is correlated to an increased blood loss (2) Whether there is a difference in markers for coagulation and fibrinolysis in peripheral venous blood compared to those in blood from the wound (3) Whether the administration of tranexamic acid modifies the fibrinolytic response. They found no direct correlation between the degree of fibrinolysis and blood loss, The administration of tranexamic acid reduced fibrinolysis in the wounds but not in the peripheral venous blood, and the postoperative blood loss was reduced by half.

Several studies have evaluated the effects of various operative techniques and treatments on TKA-associated blood loss. In 1999 **Zohar and his colleagues** conducted a study to compare postoperative blood-sparing effect of tranexamic acid versus acute normovolumic hemodilution (NVHD) after total knee replacement. They investigated 40 patients in a prospective, single blinded-study protocol In tranexamic acid group, 30 minutes before deflation of the tourniquet, an intravenous (IV) infusion of tranexamic acid, 15 mg/kg, was administered over a 30-min period. Thereafter a constant IV infusion of 10 mg/kg/hour was administered until 12 hours after deflation of the tourniquet. Before induction of anesthesia, NVHD patients were bled to a target Hct of approximately 28 %. Intravascular blood volume was mainted with lactated ringer's

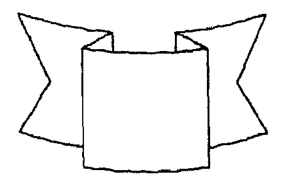
solution All autologous blood was transfused at the end of the surgery Despite autologous blood transfusion, during the early postoperative period and until the third postoperative day, the NVHD group had significantly ($P<0.01$) lower mean Hct when compared with the TA group Blood loss and blood requirement was highly significantly greater in the NVHD group than in the TA group ($P<0.0008$) They concluded that perioperative hemodynamic stability and blood sparing is superior after tranexamic acid administration when compared with normovolumic hemodilution.

A study done by **Gustav and his colleagues in 2000** demonstrated that intravenous administration of tranexamic acid started before total hip replacement decreased the perioperative bleeding to 65% of the control value. This effect was explained by reducing induced fibrinolysis as shown by a decreased FDPs level in the tranexamic acid group.

In 2000, Coker and Higgins used tranexamic acid topically in total knee arthroplasty. They found that application of tranexamic acid topically to achieve hemostasis was effective (tranexamic acid was injected into the joint cavity via the drain tube The drain tube was clamped for about 30 minutes after deflation of the tourniquet).

There was no increase in the incidence of thromboembolic complications, or other blood abnormalities. So tranexamic acid is a

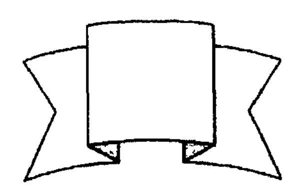
safe, and appropriate choice to reduce bleeding that follow total knee replacement. The cost-benefit ratio of this short-term tranexamic acid therapy to reduce total knee arthroplasty-associated blood loss is extremely rewarding. The cost of the whole therapy is a small fraction of the sum saved in blood products and in the use of various blood-saving techniques



Conclusion

Conclusion

Based on the results of the present study, we conclude that, (in total knee arthroplasty performed with a tourniquet), tranexamic acid 15 mg/kg, given intravenously, 5 minutes before deflation of the tourniquet, significantly ·educed blood loss by 470 ml, and blood transfusion by 433 ml without hromboembolic complications caused by total knee arthroplasty performed vith a tourniquet.



Summary

Summary

Modern total knee arthroplasty is a successful surgical procedure for the vast majority of patients, and it is now a common surgical procedure. Unfortunately total knee arthroplasty is associated with heavy bleeding that often occurs after the surgery, and it is difficult to control. Various methods and great efforts have been tried to decrease bleeding, and avoid blood transfusion with all its complications.

Tranexamic acid is a synthetic drug that inhibits fibrinolysis. In this prospective, randomized, double-blind study, we have investigated the effect of tranexamic acid (cyclokapron), on blood loss and transfusion requirements associated with total knee arthroplasty. and to see if There is any Complications.

Sixty patients of both sexes, of ASA physical status I, or II undergoing total knee arthroplasty with use of a tourniquet. The patients were randomly allocated into one of two groups.

Group one(Test Group):

This group included 30 patients. Patients of this group received, 15 mg/kg body weight, I.V. bolus dose of tranexamic acid (TA) 3-5 minutes before deflation of the pneumatic tourniquet.

Group two(Control Group):

This group included 30 patients. Patients of this group received an equal volume of placebo (normal saline) I.V. 3-5 minutes before deflation of the tourniquet.

Twenty-four hours before the operation, hemoglobin concentration (Hb(gm/l)), hematocrit value (Hct), platelet count, bleeding time (BT), activated partial thromboplastin time (APPT), Prothrombin time (PT), fibrinogen level, and fibrin degradation product (FDPs) were measured for all patients. And all these laboratory tests were repeated at eight hours and on the first and second day after the operation.

Our results confirm the beneficial effect of tranexamic acid on reduction of blood loss following total knee arthroplasty.

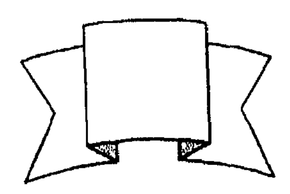
Mean blood loss in the day of surgery was 367.2 +/- 125 ml in test group, and 687.9 +/- 267.8 ml in control group. Statistical difference was highly significant ($p<0.001$). On the first day postoperatively, test patients lost a mean of 213.1 +/- 106.6 ml of blood, while control patients lost a mean of 334.3 +/- 214.3 ml; the difference was statistically highly significant ($p<0.01$). Blood loss was also significantly less in test patients than in control patients on the second day postoperatively. Mean blood loss in the former was 28.1 +/- 24.8 ml, and 57.2 +/- 125 ml in the latter ($p<0.05$). Mean total volume of blood loss after the operation was 608.5 +/- 160.2 ml in test group, and 1079.41 +/- 356.5 ml in the control group. The difference was statistically highly significant ($p<0.001$). Mean blood transfusion was significantly less in test group (250+/- 388.4 ml)as compared to control group (683.3 +/- 444.9 ml)

Ten patients from the test group (n=30) needed blood transfusion, as compared to twenty three patients from the control group (n=30) needed blood transfusion, and this was statistically significant

Despite the fewer transfusions, the postoperative hemoglobin concentrations in the treatment group were significantly higher in second P.O. day compared to control group.

None of our patients of either group manifested thromboembolic or other complications.

We conclude that tranexamic acid reduced postoperative blood loss and transfusion requirements associated with total knee arthroplasty.



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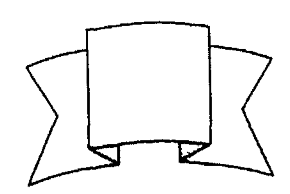
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Arabic Summary

فقد مرض المجموعة الثانية الأولي (٣٣٤,٣ ± ٢١٤,٣٠ ملليلتر) ولقد كـــان الاختلاف ذو اهمية أحصائية .

ولقد كان فقـد الـدم فـي مـرضي مجموعة الاختبار أقـــل عنـــه فـــي مرضي مجموعة التحكم في اليوم الثاني . وكـــان الدم المفقود في الأولي الأولي (٢٨,١ ± ٢٤,٨ ملليلتر) وفي الثانيـــة (٥٧,٢ ± ١٢٥ ملليلـــتر) وقـــــد كـــان الاختلاف ذو اهمية إحصائية .

وكـــان النـــزيف الدمـــوي الكلـــي بعد العملية في مجموعة الاختـــــبار (٦٠٨,٥ ± ١٦٠ملليلتر)وفي مجموعة التحكم (١٠٧٩,٤١ ± ٣٥٦,٥٠ ملليلتر) وكذلك معدل نقل الدم في مجموعة الاختبار ٢٥٠ ± ٣٨٨ ملليلتر بالمقارنــــه بمجموعة التحكم ٦٨٣,٣ ± ٤٤٤,٩ ملليلتر . احتاجت عشرة مرضي مــــن مجموعة الاختبار الي نقل دم بينما ٢٤ مريضاً في مجموعة التحكم . وبـــالرغم من ذلك كان معدل نسبة الهيموجلوبين في مجموعة الاختبار أعلـــي عنـــه فـــي مجموعة التحكم ولم تحدث اية مشاكل او أعراض جانبية للعقـــار فـــي أي مـــن المجموعتين .

ونستخلص من ذلك ان عقار الترانكسيميك يقلل من النزيف الدموي ونقـــل الدم بعد عملية تغيير مفصل الركبة .

المجموعة الثانية (مجموعةالتحكم) :-

- وتحتوي ايضاً هذه المجموعة علـــي ٣٠ مريـض . اعطينــا هــذه المجموعة محلول ملح بنفس معدل حمض الترانكسيميك وفــي نفــس التوقيت .

وفي اليوم السابق للعملية قمنا بقياس :-

- نسبة الهيموجلوبين
- تركيز الهيموجلوبين
- عدد الصفائح الدموية
- وقت النزيف
- وقت برثرومبين
- وقت الثرومبوبلاستين
- مستوي فيبرونيجين في الدم
- مستوي منتجات تكسير الفيبرين

ويعاد أجراء هذه الاختبارات بعد ٨ ساعات وبعد يوم وبعـــد يوميـــن مـــن اجراء العملية .

تؤكد دراستنا التأثير الفعال لحمض الترانكسيميك في تقليل الدم المفقود فـــي تغيير مفصل الركبه .

في نفـــس يوم الجراحة كـــانت كميـــة الـــدم المفقود في المجموعة الأولي (٣٦٧,٢ ± ١٢٥ ملليلتر) بينـــما فقد مرضي المجموعـــــة الثانيـــة الأولـــي (٦٨٧,٩ ± ٢٦٧,٨ ملليلتر) ، ولقد كان الأختلاف ذو اهمية أحصائية . لقد فقـد مرضي المجموعة الأولي في اليوم الأول (٢١٣,١ ± ١٠٦,٦٠ ملليلتر) بينمـــا

الملخص العربي

تعد عملية تغيير كامل لمفصل الركبه عملية جراحية ناجحة لاغلب المرضي كما انها تعد الأن من العمليات الجراحية المعتادة ولسوء الحظ ترتبط عملية تغيير مفصل الركبه بنزيف شديد والذي غالباً ما يحدث بعد اجراء الجراحة ويصعب التحكم فيه.

تبذل الكثير من الجهود والطرق المختلفة للتقليل من كمية النزيف وتجنب نقل الدم بكل مشكلاته .

يعد حمض الترانكسيميك عقار صناعي يقلل من تكسير الفيبرنوجين - وفي هذه الدراسة العشوائية قمنا بدارسة تأثير عقار الترانكسيميك في تقليل النزيف الدموي وتقليل الدم بعد عملية تغيير مفصل الركبة .

ولقد اجريت هذه الدراسة علي ٦٠مريضاً من الجنسين لعمل عمليه تغيير كامل لمفصل الركبة بأستخدام التورنيكية ولقد قسموا الي مجموعتين .

المجموعة الاولي (مجموعة الاختبار) :-

- وتحتوي هذه المجموعة علي ٣٠ مريض قمنا باعطاء هذه المجموعة ١٥مجم/كجم من وزن المريض من حمض الترانكسيميك في الوريد قبل فك التورنيكيه بحوالي ٣ : ٥ دقائق .

تقييم تاثير حمض الترانكسميك (سيكلوكابرون) علي النزيف الدموي اثناء وبعد عمل عملية تغير كامل لمفصل الركبة

رسالة مقدمة من

الطبيب / خالد محمد عبدالله عبد السلام

بكالوريوس الطب والجراحة - ماجستير وزمالة عربية في التحدير

توطئة للحصول على درجة الدكتوراه في التخدير

تحت إشراف

أ . د / بهيرة محمد توفيق

استاذة التخدير والرعاية المركزة

كلية الطب - جامعة عين شمس

أ . د / مديحة متولي زيدان

استاذة التخدير والرعاية المركزة

كلية الطب - جامعة عين شمس

أ . د / عادل احمد فتحي

استاذ مساعد التخدير

كلية الطب - جامعة عين شمس

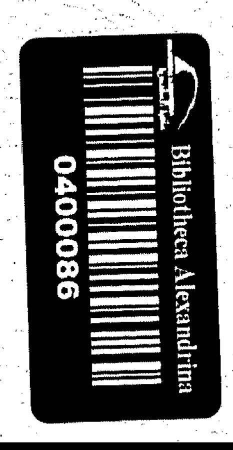
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